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X-Ray Structures of the Universal Translation Initiation Factor IF2/eIF5B: Conformational Changes on GDP and GTP Binding

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ABSTRACT: X-ray structures of the universal translation initiation factor IF2/eIF5B have been determined in three states: free enzyme, inactive IF2/eIF5B•GDP, and active IF2/eIF5B•GTP. The “chalice-shaped” enzyme is a GTPase that facilitates Met-tRNA_i binding, ribosomal subunit joining and in all three kingdoms of life. The conserved core of IF2/eIF5B consists of an N-terminal G domain (I) plus an EF-Tu-type beta-barrel (II), followed by a novel alpha-beta-alpha sandwich (III) connected via an alpha-helix to a second EF-Tu-type beta-barrel (IV). Structural comparisons reveal a molecular lever, which amplifies a modest conformational change in the Switch 2 region of the G domain induced by Mg⁺⁺/GTP binding over a distance of 90Å from the G domain active center to domain IV. Mechanisms of GTPase function and ribosome binding are discussed.